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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 09/544,108
Filing Date: April 06, 2000
Appellant(s): SHERMAN, KENNETH ELIOT

Caroline Nash
For Appellant

EXAMINER'S ANSWER

The examiner's answer mailed December 8, 2008 was returned by the Board of Appeals because the headings were not in the correct order. Aside from that correction, this examiner's answer is identical that previously mailed.

This is in response to the appeal brief filed July 15, 2008 appealing from the Office action mailed April 15, 2008.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

The following is a listing of the evidence (e.g., patents, publications, Official Notice, and admitted prior art) relied upon in the rejection of claims under appeal.

Huang et al.(Virologica Sinica, 1990, Vol. 5, p. 69-73) Chinese document is of record on 1/24/2007 and English translation of Huang et al. is of record on 3/8/2007

Hoofnagle et al. (Seminars in Liver Disease, 1989, Vol. 9, p. 259-263) of record in IDS of 5/6/2002)

5,273,963 MOODY 12-1993

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Rejection of Claims 1, 3-6, and 25 under 35 U.S.C. 103(a) as being unpatentable over Huang et al. (Virologica Sinica, 1990, Vol. 5, p. 69-73) and Hoofnagle et al. (Seminars in Liver Disease, 1989, Vol. 9, p. 259-263) in view of Moody et al. US Patent 5,273,963).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3-6, and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Huang (Virologica Sinica, 1990, Vol. 5, p. 69-73, the English translation of Huang et al. is of record on 3/8/2007) and Hoofnagle et al. (Seminars in Liver Disease, 1989, Vol. 9, p. 259-263 of record in IDS of May 6, 2002) in view of Moody et al. (US Patent 5,273,963).

Claims are drawn to a method of treating a mammal infected with hepatitis C virus comprising administering an anti-hepatitis C effective amount of interferon-α, concurrently or sequentially with administering thymosin-α. In dependent claims, interferon is interferon α-2b produced by recombinant DNA technology, the range of interferon administered is between one million and about three million units per administration, the dose of thymosin-α is about 1500 to about 1700 microgram, and the thymosin fragment is selected from the group consisting of C-terminal 4-28, C-terminal 1-8, N-terminal 1-14 and N-terminal 1-20.

Huang et al. teach a method of treating humans infected with hepatitis B comprising administering a combination of interferon-α and thymosin (see the entire document, particularly page 8 of the English translation). Huang et al. teach that the antiviral mechanism of interferon is to restrain virus replication while thymosin promotes immature T cells to become immune-active mature T cells. Huang et al. teach that thymosin increases the immune function of T cells, enhances the antiviral effect of interferon and induces the production of interferon (see page 10 of the English

translation). Thus, Huang et al. teach that the thymosin enhances the antiviral effect of interferon. Huang et al. does not teach using combination of interferon-α and thymosin in treatment of hepatitis C infection. Huang et al. does not expressly teach that the thymosin is thymosin-α.

Hoofnagle et al. teach a method of treating humans infected with hepatitis C comprising administering two to five million units of recombinant interferon-α, specifically interferon-α -2b (see the entire document, particularly page 260 Initial Studies).

Moody et al. teach an immunopotentiating effect of thymosin-α administered concurrently with chemotherapy in treatment of various cancers, thymosin-α enhances the growth and differentiation of T cells (see the entire document, particularly claims 1-13 and column 3, lines 1-18). Moody et al. teaches the thymosin fragments: C-terminal 4-28, C-terminal 1-8, N-terminal 1-14 and N-terminal 1-20 fragment and their significance for therapeutic use (see column 6, lines 17-21).

Based on the teachings of Hoofnagle, Huang and Moody, it would have been *prima facie* obvious to the skilled artisan at the time of the present invention to modify the method of Hoofnagle, who teaches treating hepatitis C infection with interferon-α to add Huang's thymosin and particularly Moody's thymosin- α to treat hepatitis C infection.

One of ordinary skill in the art would have been motivated to modify the method of Hoofnagle to add thymosin- α to treat hepatitis C infection because Huang et al. have shown that thymosin strengthens the antiviral effect of interferon-α by inducing

production of interferon and by generating active immune T cells (see page 10 of the English translation) and because Moody et al. have shown that thymosin- α acts to enhance the growth and differentiation of T cells. Because Huang et al. and Moody et al. have shown that thymosin enhances the antiviral effect of interferon and acts to enhance the growth and differentiation of T cells, the skilled artisan would have been motivated to provide a method of treating hepatitis C infection with the combination of thymosin-α and interferon-α, as opposed to using interferon- α alone. One would have been motivated to use the thymosin fragments such as C-terminal 4-28, C-terminal 1-8, N-terminal 1-14 and N-terminal 1-20, in the composition comprising thymosin and alpha interferon, because Moody et al. teach that these particular thymosin fragments have been identified to have therapeutic significance as immunopotentiators. With respect to particular doses of thymosin-α, it would have been within the ability of ordinary artisan to adjust the doses of thymosin-α in the composition. Thus the doses of compositions would have been obvious absent any unexpected results.

One would have had a reasonable expectation of success to treat hepatitis C infection with interferon-α concurrently or sequentially with administering thymosin-α because hepatitis C infection has been successfully treated with interferon-α, as evidenced by Hoofnagle et al. and because thymosin and particularly thymosin-α has been shown to enhance the effects of interferon-α and to have an immuno-potentiating effect as evidenced by Huang et al and Moody et al.

Thus the present method would have been *prima facie* obvious to the skilled artisan at the time the invention was made.

(10) Response to Argument

Appellant's arguments have been fully considered but fail to persuade.

Appellant submits that Appellant has found that improved results are achieved in treatment of hepatitis C virus infection with a combination therapy over using either interferon-α or thymosin-α alone. Appellants argue that none of the references, whether taken alone or together suggest the use of interferon- α together with thymosin- α as a sustainable and effective means for treating hepatitis C.

In response to Appellant's arguments, the Office maintains that the combination of the prior art references yields predictable results and that the improved results achieved using combination therapy comprising administering interferon-α and thymosin-α to treat hepatitis C infection presented by Dr. Sherman in the Declaration under 37 CFR § 1.132 filed January 4, 2006 and discussed by the Appellant in the Appeal Brief filed July 15, 2008 would have been expected by the skilled artisan at the time of the present invention as further discussed below.

Appellant argues that it was not known at the time of the present invention whether the interferon-α in combination with thymosin- α would have had the same effectiveness in treating hepatitis C as in treating hepatitis B. Appellant argues that the present method was not "predictable or obvious to try because of the fear of side effects canceling of one drug by the other. Extensive testing had to be performed to determine effectiveness."

In response to Appellant's arguments, the Office notes that the prior art by Hoofnagle teaches effective treatment of hepatitis C infection comprising administering

interferon-α and Huang teaches effective treatment of hepatitis B infection with interferon-α. Thus the prior art teaches that interferon-α is effective in treating hepatitis C infection as well as in treating hepatitis B infection. Because thymosin- α acts to induce more interferon-α and to activate T cells (as taught by Huang and Moody), the skilled artisan knowing that interferon-α effectively treats hepatitis C infection would have been motivated to add thymosin-α, which is known to enhance the effects of interferon-α and to provide a method of treating hepatitic C infection with a combination therapy comprising administering interferon-α and thymosin-α. Based on the known mechanism of action of thymosin-α which acts to induce production of interferon and thus enhance the antiviral effect of interferon, regardless the type of viral infection and regardless of the type of cancer, the skilled artisan would have been motivated to enhance the antiviral effect of interferon-α by adding thymosin-α in treatment of hepatitis C infection.

Appellant failed to provide evidence and/or reasoning to support the assertion that the present method was not "predictable or obvious to try because of the fear of side effects canceling of one drug by the other." The cited prior art provides evidence that thymosin enhances the effects of interferon, as discussed above (see Huang and Moody). While some drugs may cancel the effects of some other drugs, this particular combination of thymosin and interferon- α had already been shown to result in increased antiviral effect of interferon- α. Thus based on the teachings of the prior art showing that thymosin enhances the effects of interferon and that interferon effectively treats hepatitis C, the skilled artisan would have had a reasonable expectation of

success to treat hepatitis C using combination therapy comprising administering interferon- α in combination with thymosin- α.

Appellant argues that no generalized assumption would have been made by one of ordinary skill in the art that a vaccine that works for one type of hepatitis would work for the other type of hepatitis. In response to Appellant's arguments, the Office entirely agrees that in case of a vaccine against different hepatitis viruses, the skilled artisan would not have made the assumption that a vaccine that works for one type of hepatitis would work for the other type of hepatitis. That is because the skilled artisan knows that the effectiveness of a vaccine is strictly antigen specific. In contrast to vaccines against hepatitis viruses, the treatment of hepatitis B or C infection with interferon- α and thymosin- α is not antigen specific. The interferon- α and thymosin- α both act to stimulate the immune system regardless of the type of viral infection and the stimulation of T cells with interferon- α and thymosin- α is not antigen specific as evidenced by the fact that the interferon- α alone is effective in treating an infection caused by hepatitis B as well as hepatitis C (see Huang and Hoofnagle). The thymosin in the present method has a similar effect to an effect of an adjuvant or an immunomodulator in a vaccine. That means it stimulates the T cells without being restricted or specific to the type of infection. It would have been obvious to add an adjuvant or an immunomodulator to a composition that induces antigen specific response. For example, assuming that a particular immunomodulator is known in the prior art to enhance an immune response, it would have been obvious to add the immunomodulator to the prior art vaccine

composition. Hence, the known immunomodulator/adjuvant would have been expected to stimulate the immune system regardless the type of viral infection. The skilled artisan knowing that interferon- α is effective in treating hepatitis C infection would have been motivated to enhance the action of interferon- α with thymosin- α and to treat hepatitis C with the combination therapy. Thus in view of the teachings in the prior art the presently claimed method would have been obvious to the skilled artisan at the time of the present invention.

The Declaration by Dr. Sharman filed January 4, 2006 has been fully considered. Figure 2 shows the results of treatment of hepatitis C infection with the combination therapy comprising interferon- α and thymosin- α compared to the treatment with the interferon- α alone. Figure 3 shows the largest reduction in HCV RNA in patient treated with the combination compared to the patients treated with interferon- α alone. It is acknowledged that the combination therapy resulted in a higher histologic response and the higher reduction of viral RNA in patients treated with the combination therapy compared to pateints treated with interferon- α alone. However the improved result using combination therapy would have been expected at the time of the present invention, because the skilled artisan had known that thymosin- α acts on inteferon- α to increase the effects of interferon- α regardless the type of virus that infects the host (see Huang et al. and Moody et al. as discussed above). It is additionally noted that the prior art discloses effective treatment of hepatitis C infection with inteferon- α (see Hoofnagle et al cited in the present rejection). Because it has been known that thymosin- α acts to

increase the effects of interferon- α, one of ordinary skill in the art would have expected that combination therapy would have given better results over the treatment with interferon- α alone.

In conclusion, the teachings of the prior art references in combination would have yielded nothing more than predictable results of treating a mammal infected with hepatitis C comprising administering a combination of interferon- α and thymosin- α compared to the treatment with the interferon- α alone. The addition of a known element, the thymosin- α, in the method comprising treating hepatitis C with interferon- α disclosed by Hoofnagle would have yielded predictable results because thymosin- α was known to enhance the antiviral activity of interferon- α as discussed above. The skilled artisan would have had a reasonable expectation of success to treat hepatitis C infection comprising administering a combination of interferon- α and thymosin- α because skilled artisan had known that interferon- α is effective in treating hepatitis C (as evidenced by Hoofnagle) and because the skilled artisan had known that thymosin enhances the antiviral effects of interferon- α in treating hepatitis B (as evidenced by Huang).

The improved results achieved using combination therapy comprising administering interferon-α and thymosin-α to treat hepatitis C infection presented by Dr. Sherman in the Declaration under 37 CFR § 1.132 would have been expected by the skilled artisan at the time of the present invention because the effects of thymosin as an

immunomodulator to enhance the effectiveness of interferon- α have been known in the prior art as discussed above

Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the cited prior art references, and in the absence of evidence to the contrary.

For the above reasons, it is believed that the rejections should be sustained.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

Respectfully submitted,

/Agnieszka Boesen/

Examiner, Art Unit 1648

Conferees:

/Bruce Campell/
Supervisory Patent Examiner, Art Unit 1648

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Supervisory Patent Examiner, Art Unit 1649